

Effects of Aryl Hydrocarbon Receptor-Mediated Early Life Stage Toxicity on Lake Trout Populations in Lake Ontario during the 20th Century

PHILIP M. COOK,^{*,†} JOHN A. ROBBINS,[‡]
DOUGLAS D. ENDICOTT,^{†,§}
KEITH B. LODGE,^{||}
PATRICK D. GUINEY,^{⊥,¶}
MARY K. WALKER,^{○,▽}
ERIK W. ZABEL,^{○,×} AND
RICHARD E. PETERSON^{⊥,○,+}

Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, 6201 Congdon Boulevard, Duluth, Minnesota 55804, Great Lakes Environmental Research Laboratory, National Oceanographic and Atmospheric Administration, 2205 Commonwealth Boulevard, Ann Arbor, Michigan 48105-1593, Department of Chemical Engineering, University of Minnesota—Duluth, 1303 Ordean Court, Duluth, Minnesota 55812-3025, NIEHS Marine and Freshwater Biomedical Sciences Center, University of Wisconsin—Milwaukee, 600 East Greenfield Avenue, Milwaukee, Wisconsin 53204, Molecular and Environmental Toxicology Center, University of Wisconsin—Madison, 1710 University Avenue, Madison, Wisconsin 53726-4098, and School of Pharmacy, University of Wisconsin, 777 Highland Avenue, Madison, Wisconsin 53705-2222

Lake trout embryos and sac fry are very sensitive to toxicity associated with maternal exposures to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and structurally related chemicals that act through a common aryl hydrocarbon receptor (AHR)-mediated mechanism of action. The loading of large amounts of these chemicals into Lake Ontario during the middle of the 20th century coincided with a population decline that culminated in extirpation of this species around 1960. Prediction of past TCDD toxicity equivalence concentrations in lake trout eggs (TEC_{egg}S) relative to recent conditions required fine resolution of radionuclide-dated contaminant profiles in two sediment cores; reference core specific biota—sediment accumulation factors (BSAFs) for TCDD-like chemicals in lake trout eggs; adjustment of the BSAFs for the effect of temporal

changes in the chemical distributions between water and sediments; and toxicity equivalence factors based on trout early life stage mortality. When compared to the dose—response relationship for overt early life stage toxicity of TCDD to lake trout, the resulting TEC_{egg}S predict an extended period during which lake trout sac fry survival was negligible. By 1940, following more than a decade of population decline attributable to reduced fry stocking and loss of adult lake trout to commercial fishing, the predicted sac fry mortality due to AHR-mediated toxicity alone explains the subsequent loss of the species. Reduced fry survival, associated with lethal and sublethal adverse effects and possibly complicated by other environmental factors, occurred after 1980 and contributed to a lack of reproductive success of stocked trout despite gradually declining TEC_{egg}S. Present exposures are close to the most probable no observable adverse effect level (NOAEL TEC_{egg} = 5 pg TCDD toxicity equivalence/g egg). The toxicity predictions are very consistent with the available historical data for lake trout population levels in Lake Ontario, stocking programs, and evidence for recent improvement in natural reproduction concomitant with declining levels of persistent bioaccumulative chemicals in sediments and biota.

Introduction

The Lake Ontario ecosystem has been affected in many ways by human activities since settlement of the region altered the watershed through clearing of forests and construction of dams on tributaries in the 1800s. Subsequently, growth of agriculture, increased commercial fishing, and introduction of exotic species created additional stress on populations of native fish. Despite these stresses, lake trout (*Salvelinus namaycush*) and other deep water fish species were abundant in the 1920s (1). Declines in these fish populations, which began in the 1930s, have been attributed to over-harvesting and predation by the sea lamprey (*Petromyzon marinus*), although the lamprey was present in Lake Ontario since the 1830s (2). By 1960, lake trout in Lake Ontario were virtually extirpated (3). The disappearance of other deep water species, such as the fourhorn sculpin (*Myoxocephalus quadricornis*), cannot be attributed to fishing or lamprey predation (1). Failure of lake trout stocking in the 1960s to establish a sustainable population has been attributed to sea lamprey predation and incidental commercial harvest (4). In conjunction with sea lamprey larvicide treatments of Lake Ontario tributaries that began in 1971, attempts to re-establish lake trout populations through stocking of yearlings continued. Adult lake trout were present in the late 1970s; however, no sac fry from natural reproduction were observed until 1986 (5). In 1995, evidence of survival of young lake trout to 1 yr was reported (6), and the accumulated signs of general ecosystem recovery indicated that significant recruitment of lake trout through natural reproduction might be achieved by the year 2000 (4). Young lake trout from natural reproduction have continued to be observed to the present, but changes in sampling methodology that caused fewer young fish to be captured make it difficult to compare annual survival rates (7).

With sea lamprey numbers reduced, water quality improved, and fishing regulated, the post-1970 failure of stocked lake trout to produce viable young has prompted investiga-

* Corresponding author phone: (218)529-5202; fax (218)529-5003; e-mail: cook.philip@epa.gov.

† U.S. Environmental Protection Agency.

‡ National Oceanographic and Atmospheric Administration.

§ Present address: Great Lakes Environmental Center.

|| University of Minnesota—Duluth.

⊥ University of Wisconsin—Milwaukee.

¶ Present address: S. C. Johnson & Son, Inc.

○ University of Wisconsin—Madison.

▽ Present address: College of Pharmacy, University of New Mexico.

× Present address: Minnesota Department of Health.

+ School of Pharmacy, University of Wisconsin.

tions of other potential impediments for reproduction and survival of young. These have included assessments of interstitial water quality in spawning areas (8), genetic sufficiency of stocked lake trout strains (9), water temperatures at spawning (10), and alewife predation on lake trout eggs and fry (11). Because the decline and loss of lake trout populations coincided with the addition of many anthropogenic chemicals to the water, sediment, and biota, we have investigated a possible etiology involving chemical toxicity for Lake Ontario, as has been considered for Lake Michigan (12).

In Lake Ontario persistent hydrophobic chemicals, such as polychlorinated biphenyls (PCBs), tend to be evenly distributed throughout sedimentation basins (13). PCBs, polychlorinated dibenzo-*p*-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs) bioaccumulate in lake trout throughout the Great Lakes (14, 15). PCBs have been shown to biomagnify in the Lake Ontario food web so that lake trout at the top of the aquatic food chain have the greatest concentrations in tissues (16). Prediction of the bioaccumulation of TCDD and related chemicals in embryos is a critical step in assessing toxicity risks to fish exposed to PCDDs, PCDFs, and PCBs during early life stages (17).

While there are 419 possible PCDD, PCDF, and PCB congeners, only 21 are known to be highly toxic to fish. These potent chemicals have chlorine substitution patterns that create molecular geometries with planar conformations similar to that of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). Collectively, these chemicals are referred to as aryl hydrocarbon receptor (AHR) agonists because their similarity in molecular size and conformation allows them to act by an identical AHR-mediated mechanism (18). Genes for AHRs and other proteins that participate in AHR signaling in vertebrate species have been identified and characterized in both bony and cartilaginous fishes (19) and are expressed during early life stage development in fish (20, 21). PCDDs, PCDFs, and PCBs that act as AHR agonists produce an identical spectrum of toxicity in trout early life stages (22–24). In early life stages of lake trout, the dose–response relationship for TCDD-induced cytochrome P4501A expression in vascular endothelial cells, a classic AHR-mediated response in fish, parallels that for TCDD-induced sac fry mortality associated with cardiovascular dysfunction (25).

Mortality associated with signs of toxicity resembling blue sac disease, a noninfectious, edematous condition first observed when trout eggs were exposed to ammonia (26), was later observed for sac fry raised from fertilized eggs collected from Lake Ontario lake trout during the period of 1977–1984 (27). Subsequently, lake trout sac fry (Figure 1) were found to be extremely sensitive to TCDD, following exposure of fertilized eggs, with mortality following signs of toxicity that resembled the blue sac syndrome (28, 29). Maternal transfer of TCDD to lake trout eggs results in sac fry mortality when concentrations in the eggs exceed 30 pg/g wet weight (28, 30, 31). TCDD and other AHR agonists interact in an additive fashion to cause sac fry mortality in trout (32, 33). Thus, assessment of toxicity risks associated with the complex mixture of AHR agonists in Lake Ontario must consider the additive contributions of each chemical. A complicating risk factor in recent years has been the presence of another mortality syndrome in lake trout fry at swim-up. This syndrome is associated with thiamine deficiency in embryos (34) but is thought to not be directly associated with organochlorine contaminants in the eggs (35, 36).

In 1978, the Great Lakes Water Quality Agreement between Canada and the United States provided for the establishment of ecosystem objectives for protection of the Great Lakes basin ecosystem. The lake trout, as the major native top trophic level predator fish, was selected as a key species for monitoring the ecological condition of the large oligotrophic

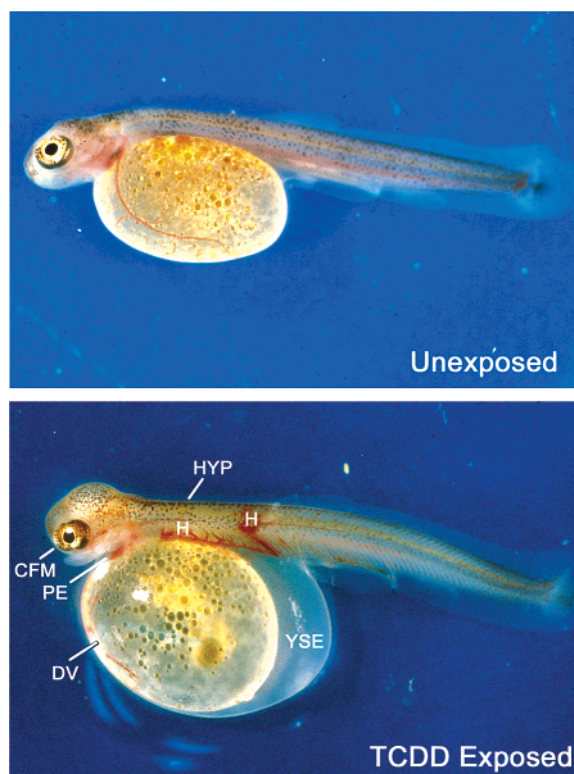


FIGURE 1. Lake trout sac fry unexposed (top) and exposed (bottom) as fertilized eggs to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). Sac fry exposed to TCDD have external signs of toxicity, including yolk sac edema (YSE) and pericardial edema (PE) associated with damage to vascular tissues (DV), hemorrhaging (H), craniofacial malformations (CFM), and hyperpigmentation (HYP), which lead to death prior to the swim-up stage of development.

portions of the Great Lakes (37). Although habitat alteration and introduction of exotic species may explain the disappearance of some fish species in Lake Ontario, lake trout in the Great Lakes have a low risk of extinction when these factors are analyzed in the context of the species' life history (38). Lake trout are, however, the most sensitive fish species known for early life stage mortality associated with exposure to TCDD and related chemicals (39). Fitzsimons (40), however, concluded that concentrations of TCDD in lake trout eggs, which induce overt early life stage mortality (i.e., greater than 30 pg/g egg), are much greater than recent concentrations measured in feral lake trout eggs from Lake Ontario. Thus, while lake trout mortality due to sea lamprey and human predation have been controlled in order to create sustainable lake trout populations, the impacts of chemical exposures over time on feral lake trout reproduction and early life stage survival have remained uncertain. In our current assessment of this problem, measurement end points included chemical exposures as concentrations of PCDD, PCDF, and PCB congeners in feral lake trout eggs, variation of exposure levels since 1920, and doses in eggs associated with sac fry mortality responses for each potentially toxic AHR agonist. We then sought to compare toxicity hazard predictions based on these data and the additive toxicity equivalence model to observations of relevant effects and population trends for lake trout in Lake Ontario. The criteria recently proposed by Barnthouse et al. (41) for testing hypotheses that chemical exposures have reduced reproductive success of fish populations were exceeded in this study by inclusion of species specific toxicity data and rigorous analysis of population level responses over a long period of time.

Materials and Methods

Sample Collection. *Fish.* Lake trout tissue and egg samples collected at different locations in the years of 1991, 1990, 1988, 1987, 1984, and 1978 were utilized in this study to establish recent trends in chemical concentrations in Lake Ontario lake trout eggs. Lake trout and other species were collected throughout Lake Ontario in 1987 and analyzed for TCDD for the U.S. EPA Lake Ontario TCDD Bioaccumulation Study (42), which preceded and facilitated this study. Concentrations of TCDD in 5–7-year-old lake trout from sampling locations throughout the lake were found to not be significantly different (ANOVA). Three 7-year-old lake trout collected by the New York Department of Conservation in eastern Lake Ontario at spawning time in 1988 were used as the primary data set in this study for establishing bioaccumulation factors for embryos. These fish were received from Dr. Cliff Schneider of the Cape Vincent Fisheries Research Station on November 4, 1988, as frozen samples of whole fish and liver individually wrapped in aluminum foil in plastic bags and as eggs in glass jars. The loose eggs were removed from ovaries without fertilization or water hardening. Other lake trout samples were utilized to analyze recent exposure trends and consisted of whole trout collected by the U.S. Fish and Wildlife Service from eastern Lake Ontario in 1977, 1984, and 1987 (kindly provided by D. W. Kuehl, U.S. EPA), and trout egg samples from 1990 and 1991 used for determinations of early life stage mortality responsiveness to TCDD by Guiney et al. (31).

Sediments. A rectangular box core was collected on August 10, 1987, at the eastern end of the Rochester Basin in Lake Ontario. The site (LO87-20, latitude 43°38.10' N; longitude 76°39.24' W) was located in an area of high net sediment accumulation (43) less than 4 km from site G32 where box cores were collected in 1981 (44, 45), in 1992 (46), and in 1993 (47). This site was chosen to best represent historical trends for persistent hydrophobic organochlorine contaminants associated with the primary lake trout habitat in the eastern region of Lake Ontario. A second box core (LO87-D16) was collected at a site (latitude 43°27.20' N; longitude 78°16.76' W) located closer to the mouth of the Niagara River on the U.S. side of the Mississauga Basin. Two subcores were taken 10 cm apart near the center of each box core with minimal disturbance of sediments by insertion of 10 cm i.d. clear butyrate tubes. Each subcore was maintained in an upright position aboard ship, slowly extruded by water pressure, and sectioned in 1-cm intervals. The sections for contaminant analyses (E subcore) were placed in hexane-rinsed glass jars with foil-lined lids and frozen for shipment to U.S. EPA, Duluth, MN. The sections for radionuclide analyses (G subcore) were placed in rinsed polyethylene bottles and frozen for transport to the Great Lakes Environmental Research Laboratory (GLERL), NOAA, Ann Arbor, MI. Following chemical analyses at U.S. EPA in Duluth, portions of unprocessed dried sediment were also sent to GLERL for analysis of ^{137}Cs in order to correct for slight systematic differences between section thicknesses of E and G subcores.

Contaminant Analyses. Procedures used at the U.S. EPA in Duluth for determination of concentrations of individual PCDDs, PCDFs, and nonortho-chlorinated biphenyls by high-resolution gas chromatography/high-resolution mass spectroscopy (HRGC/HRMS) using ^{13}C -labeled internal standards have been described previously (31, 48, 49). Ortho-chlorinated biphenyls were analyzed by GC/ECD using procedures and criteria established for the U.S. EPA's Green Bay Mass Balance Study (50). A more detailed description of the methods used for storage; extraction; cleanup; and analysis of tissue, egg, and sediment subcore section samples is available as Supporting Information. One section (7–8 cm) of sediment core LO87-20, corresponding to the 1972–1974 time period,

was only analyzed for TCDD (sample lost before total congener analysis) so concentrations of other congeners were estimated based on ratios to TCDD measured in the two adjacent core sections.

Radionuclide Dating of Sediments. Two radionuclides, ^{210}Pb (naturally occurring) and ^{137}Cs (from nuclear weapons atmospheric test fallout in the 1960s), were measured in 1-cm increments from each E subcore in order to determine the time scale for changes in PCDD, PCDF, and PCB concentrations in Lake Ontario sediments. Frozen samples were weighed, freeze-dried, re-weighed, and then desegregated by mortar and pestle. Aliquots up to 20 g were packed in vials to standardized geometry, counted for ^{137}Cs and ^7Be on a high-resolution Ge(Li) γ -detector calibrated with NIST-traceable standards. The short-lived, atmospherically delivered cosmogenic radionuclide, ^7Be ($t_{1/2} = 53.4$ d) was used to determine that surface sediments were recovered, as required to establish recent chronologies. For analysis of ^{210}Pb , its daughter product (^{210}Po) was extracted from separate 2-g portions of sediment using 125 mL of HCl (50% v/v) containing a well-determined amount of ^{209}Po as a yield monitor. Over 1-week-long extraction time, several milliliters of 30% H_2O_2 (20 mL total) were periodically added. Subsequently, the mixture was centrifuged; the supernatant was decanted, filtered, and adjusted to pH 1.5; and the two Po isotopes were spontaneously plated from solution onto polished copper disks (51) that were then counted by high-resolution α -spectroscopy.

The ^{210}Pb method for establishing chronologies of recent sediments (52), applied to lake sediments by Krishnaswami et al. (53) and used in the Great Lakes by Robbins and Edgington (54, 55), was used in this study for core LO87-20 based on comparison and analysis of ^{210}Pb and ^{137}Cs data for cores LO81-G32 (44, 45) and LO93-G3 (47). Results from two contrasting dating models were compared; one based on a constant rate of supply (CRS) of excess ^{210}Pb to sediments (56–58) and the other based on a variable rate of supply (VRS) of excess ^{210}Pb to sediments. In the VRS model, the net mass accumulation rate consists of a constant rate of supply of externally loaded materials, principally clays and some refractory organic matter, plus a variable rate of supply of authigenic (internally produced) constituents, primarily organic matter, calcium carbonate, and biogenic silica (45). A more detailed description of the CRS and VRS methods is available as Supporting Information.

Risk Assessment Model

The conceptual model and data analysis used for this assessment of toxicity risks of TCDD and related chemicals to lake trout in Lake Ontario followed the U.S. EPA's guidelines for ecological risk assessment (59) and recommendations for application of TCDD toxicity equivalence factors (TEFs) to fish and wildlife (60). The problem formulation is outlined in the Introduction.

Characterization of Early Life Stage Exposures. Doses responsible for dioxin toxicity effects in lake trout sac fry are best related to concentrations of AHR agonists accumulated in eggs through maternal transfer (17). Elimination of TCDD and related chemicals by lake trout embryos and sac fry is slow, so most of the maternal dose is retained during early life stage development (23, 29). Thus, measured or predicted concentrations of PCDDs, PCDFs, and PCBs in lake trout eggs were used to model overall early life stage exposure. The potential for increased toxicity associated with post-maternal exposures of lake trout embryos, sac fry, and alevins from water or food exposure under environmental conditions is uncertain at this time.

When lake trout egg samples were not available for direct analysis, concentrations of PCDDs, PCDFs, and PCBs in eggs were predicted from concentrations in whole lake trout or

surrogate species for years when lake trout were absent. Since relevant contaminant data were unavailable for any biota prior to 1971, concentrations in lake trout eggs were determined from concentrations in sediment. Biota sediment accumulation factors (BSAFs) (61) were used to relate measurements of sediment organic carbon-normalized concentrations (C_{soc}) of PCDD, PCDF, and PCB congeners to lipid-normalized concentrations in lake trout eggs (C_{egg}):

$$\text{BSAF}_{\text{egg}} = \frac{C_{\text{egg}}}{C_{\text{soc}}} \quad (1)$$

BSAFs for PCDDs and PCDFs not detected in eggs or fish but present in the sediment were based on one-half the level of detection obtained for the specific tissue sample. Intrinsic differences in bioaccumulation potential (including effects of bioavailability, metabolism, and biomagnification) were indicated by measured BSAFs, which are species, life stage, and site-specific.

The exposure model used in this assessment assumes that the timing of maximum and declining lake trout exposures, and thus C_{egg} s, roughly paralleled the temporal trends of chemical concentrations in sediment cores from central and eastern sedimentation basins in Lake Ontario. Prediction of C_{egg} s prior to 1972 from radionuclide-dated 1-cm sections of the two sediment cores required adjustment of recently measured $\text{BSAF}_{\text{eggs}}$ (1978–1988) for the earlier conditions in which relatively larger concentrations of the chemicals existed in water with respect to concentrations in surface sediments. For a given C_{soc} , C_{egg} will increase if C_{w}^{fd} increases because more chemical will be available for uptake through the gills and from the pelagic food chain diet. Thus, BSAFs for fish exposed to persistent hydrophobic organic chemicals will increase with increases in concentrations of freely dissolved chemicals in water (C_{w}^{fd}) and consequent decreases in Π_{socw} , the sediment–water column concentration quotient (62, 63):

$$\Pi_{\text{socw}} = \frac{C_{\text{soc}}}{C_{\text{w}}^{\text{fd}}} \quad (2)$$

The degree to which BSAFs increase when Π_{socw} decreases is affected by the relative importance of benthic and pelagic food chains for the fish species. Variation of BSAFs for fish with Π_{socw} is slight when exposure to very hydrophobic ($\log K_{\text{ow}} > 6$) chemicals occurs through benthic food chains (64), as is the case for lake trout in Lake Ontario. Adult lake trout in Lake Ontario feed predominantly on smelt and alewife, which are partially linked to benthic food organisms (16). The degree of BSAF variation over time was nevertheless important in this study because achievement of maximum accuracy for retrospective use of the BSAFs measured for 1978–1988 required adjustment for earlier differences in Π_{socw} .

Post-1970 concentration profiles in sediment cores are consistent with a 90% decrease in external loadings of PCDDs, PCDFs, and PCBs to Lake Ontario, leading to three decades of exposure conditions strongly associated with contaminated sediments. Previously, from 1940 to 1970, increases in concentrations of hydrophobic chemicals such as PCBs in water were associated with slower increases in concentrations in sediment and an intermediate response for increasing concentrations in lake trout (65). BSAFs for adult lake trout were probably slightly larger before 1970 when fugacity ratios ($\Pi_{\text{socw}}/K_{\text{ow}}$) between sediment and water were ≤ 1 for PCDDs, PCDFs, and PCBs rather than > 5 as indicated for the 1980s from PCB concentrations in water and sediment (66). Therefore, $\text{BSAF}_{\text{eggs}}$ for years prior to 1974 were adjusted for variations in Π_{socw} . The Π_{socw} values were predicted from

estimated chemical loading changes with a dynamic mass balance simulation of significant processes affecting sediment–water exchange of chemicals with different hydrophobicities (67). The model indicated that the chemical distributions between sediment, water, and fish would result in pre-1970 BSAFs for lake trout, which were 2–3 times greater than recent BSAFs. Thus, pre-1970 $\text{BSAF}_{\text{eggs}}$ were set at two times the 1978–1988 measured $\text{BSAF}_{\text{eggs}}$ to account for the effect on C_{egg} of Π_{socw} conditions prior to 1970. Calculations of C_{egg} s after 1970 utilized the 1978–1988 measured $\text{BSAF}_{\text{eggs}}$, except for 1970–1972 and 1972–1975 for which $\text{BSAF}_{\text{eggs}}$ were set at 1.7 and 1.4 times the 1978–1988 values, respectively.

Characterization of Ecological Effects. The average C_{egg} at which TCDD induced mortality of lake trout sac fry in bioassays was not significantly greater than controls was approximately 30 pg TCDD/g wet egg (23, 29–31). One hundred percent mortality occurred when concentrations of approximately 100 pg TCDD/g wet egg were reached. Gross pathologies observed for brook trout (*Salvelinus fontinalis*) sac fry from eggs exposed to nonlethal doses of TCDD through maternal transfer (68) suggest that survival of lake trout sac fry or alevins in the environment may be reduced when TCDD C_{egg} s are less than 30 pg/g. Integration of toxicity data with the exposure and bioaccumulation predictions required that toxicities relative to TCDD be evaluated for each chemical in lake trout eggs that may have contributed to early life stage mortality through an AHR-mediated mechanism.

Potencies of chemicals for AHR-mediated effects have been measured relative to TCDD and expressed as TCDD toxicity equivalence factors (TEFs) (69). Recently, a distinction has been made between TEFs, which represent consensus values derived from the available relative potency data by experts under the World Health Organization (WHO) (70), and relative potency factors (RPFs), which may be chosen from individual or multiple relative potency data points. RPFs may be used to increase species and end point specificity. This toxicity equivalence analysis of lake trout early life stage mortality risks in Lake Ontario using WHO TEFs for fish is particularly direct and robust because the TEFs are based on relative potency data reported for rainbow trout (*Oncorhynchus mykiss*) early life stage mortality following embryo exposures (22, 24). Thus, since the TEFs are based on ratios of $\text{LC}_{\text{egg}50}$ (chemical concentration in trout embryos associated with 50% lethality prior to the alevin phase of development) between TCDD and each chemical, we will refer to them specifically as TEF_{eggs} . The applicability of the rainbow trout TEF_{eggs} for predicting early life stage toxicity to lake trout has been further demonstrated for PCB 126 [the most potent PCB congener (23)] and a complex mixture of PCDD, PCDF, and PCB congeners (32).

The TCDD toxicity equivalence concentration of an individual chemical accumulated in a lake trout egg (tec_{egg}) is the product of the chemical's TEF_{egg} times the concentration of the chemical in the egg (pg/g wet wt). The total TCDD toxicity equivalence concentration in the egg (TEC_{egg}) equals the sum of all tec_{eggs} . Historical TEC_{eggs} , for exposures to complex mixtures involving (n) AHR agonists, were determined with eq 3 from sediment organic carbon-normalized concentrations (C_{soc}) measured in dated sediment layers. The fraction lipid in lake trout eggs (f_{egg}) is a constant equal to 0.08:

$$\text{TEC}_{\text{egg}} = \sum_{i=1}^n (\text{tec}_{\text{egg}})_i = \sum_{i=1}^n (C_{\text{soc}})_i (\text{BSAF}_{\text{egg}})_i (f_{\text{egg}}) (\text{TEF}_{\text{egg}})_i \quad (3)$$

The risk characterization step in this assessment involved application of the extensive dose–response data available for toxic effects of TCDD and related chemicals to lake trout during early life stages. The degree of early life stage mortality was calculated from TEC_{egg} values. As an indication of minimum TCDD toxicity risk to lake trout sac fry, TEC_{egg} values in the range of 30–100 pg TCDD toxicity equivalence/g wet egg were linearly equated (eq 4) to a range of 0–100% mortality:

$$\% \text{ mortality} = (TEC_{egg} - 30)(100/70) \quad (4)$$

Impacts of sublethal effects that could reduce survival of sac fry and alevins at $TEC_{eggs} < 30$ pg TCDD toxicity equivalence/g wet egg were considered. The species-specific early life stage mortality and developmental toxicity predictions were then evaluated for coherence over time with epidemiological observations of effects on lake trout reproductive success and overall population trends in Lake Ontario. Observed population trends were compared graphically to the sac fry mortality trends predicted on the basis of AHR-mediated toxicity.

Results

Sediment Core Chronology. The cosmogenic radionuclide 7Be ($t_{1/2} = 53.4$ d) is delivered to the Great Lakes from the atmosphere and adsorbed nonspecifically with high affinity by particulate matter (71). Vertically integrated amounts of 7Be in LO87-20 and LO87-D16 were 1.2 and 1.6 dpm cm^{-2} , respectively, consistent with the rate of 7Be delivery to the lake (72). This is sufficient to show that surficial sediments were recovered by the collection method. Specific activities of 7Be penetrated deeper into sediments than can be accounted for by sedimentation alone. Because of the short half-life of 7Be , depth profiles provide a lower limit for the range of sediment mixing; in this case 2 cm. Mixing could be due to natural reworking of bulk sediments by organisms and physical processes or to translocation of small amounts of surface sediments downward when inserting subcore tubes into sediments in the box core.

To establish ages for E subcore sections, it was necessary to reconstruct their dry sediment contents since these were not measured. Comparisons of specific activities (SA) of ^{137}Cs versus depth (cm) in G and E subcores for sites LO87-20 and LO87-D16 (Figure 2, panels a and c, respectively) show that peaks corresponding to maximum fallout are significantly different in the two subcores. The displacement of SA profiles in E subcores relative to G subcores is about 1 cm downward in core LO87-20 and 2 cm upward in core LO87-D-16. The displacements are due to systematic differences in the amount of dry sediment contained in the nominally 1-cm-thick sediment sections. These subcore differences can arise from systematic parallax errors in estimation of the thicknesses of sections during sampling, differential compaction on insertion of subcore tubes, and differences in recovery of fluid interfacial sediments. Their effects can be adequately corrected by proportional scaling of the cumulative weight (in $g\ cm^{-2}$) of sediment associated with G subcores (g_G). The reconstructed cumulative weight of dry sediment in E subcore sections (g_E) was determined as $g_E = \alpha g_G$, where values of α were obtained from least-squares minimization of differences in ^{137}Cs SA profiles between G and E subcores. Correction of E subcore dates with g_E produced virtually congruent subcore SA profiles for cores LO87-20 and LO87-D-16 (Figure 2, panels b and d, respectively). Optimized values of α were 0.859 and 1.34 for cores LO87-20 and LO87-D16, respectively.

Constant Rate of Supply (CRS) Analysis. Distributions of ^{210}Pb SA in three cores from eastern Lake Ontario are shown (Figure 3a) in terms of sediment section ages determined by

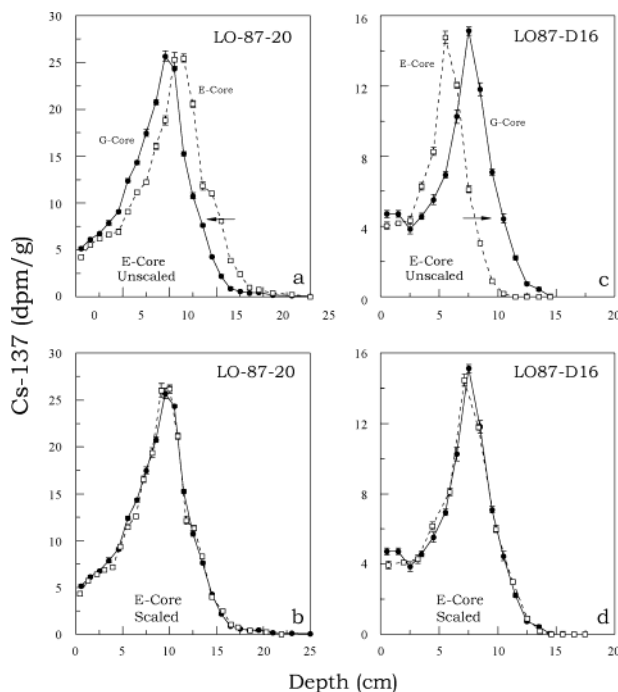


FIGURE 2. Resolution of solids mass differences between subcores used for dating (G) and chemical analyses (E). Specific activities (SA) of ^{137}Cs vs nominal depths (cm) in G subcores (solid circles) and E subcores (open squares), before and after scaling for systematic differences in dry mass content ($g\ cm^{-2}$): (a) LO87-20 before E subcore scaling (arrow); (b) LO87-20 after E subcore scaling based on 14% less solids per section than G subcore; (c) LO87-D16 before E subcore scaling (arrow); (d) LO87-D16 after E subcore scaling based on 34% more solids per section than G subcore.

the CRS method. Vertical axes (not shown) for LO81-G32 and LO93-G32 were proportionately scaled to the LO87-20 axis. The agreement between ^{210}Pb SA distributions for cores collected in 1981, 1987, and 1993 is striking. All indicate a ^{210}Pb SA plateau between CRS dates of 1965–1980 (shaded). The rise in ^{210}Pb SA after 1980 is quite clear in core LO87-20 (solid circles) and very well-developed in core LO93-G32 (open diamonds). These results show that the ^{210}Pb SA plateau cannot be due to steady-state mixing as suggested by Eisenreich et al. (44). Rather, it is associated with increased deposition of organic matter and calcium carbonate as indicated in Figure 3b by the long-term trend in the fraction of sediment soluble in acid peroxide. This fraction increases throughout the 20th century, including the period of 1965–1980 (shaded area). Given this structure, it seems unlikely that the ^{210}Pb SA plateau could be due to an episode of rapid sediment mixing or slumping.

Sediment accumulation rates versus age, as calculated by CRS, are consistent between cores LO87-20 and LO81-G32 (Figure 3c). Pre-1965 rates are about $0.12\ g\ cm^{-2}\ yr^{-1}$, increase 50% between 1965 and 1980 (shaded region) to $0.18\ g\ cm^{-2}\ yr^{-1}$, and start to decline beyond 1980. Inspection of the ^{210}Pb SA profile (Figure 3a) for core LO93-G32 (47) indicates that this decline continued between 1987 and 1993.

Distributions of the fallout radionuclide, ^{137}Cs ($t_{1/2} = 30.2$ yr), used to independently verify sediment age assignments based on ^{210}Pb (73), are shown in Figure 3d along with records of monthly atmospheric fallout to the Great Lakes region (74). Compared with the fallout records, ^{137}Cs distributions are much broader. Since ^{137}Cs is strongly bound to sediment particles (clay minerals), broadening cannot be due to post-depositional migration of the radionuclide. Rather it is due to system time averaging processes external to sediments (75) that produce slow post-fallout declines in activity. That

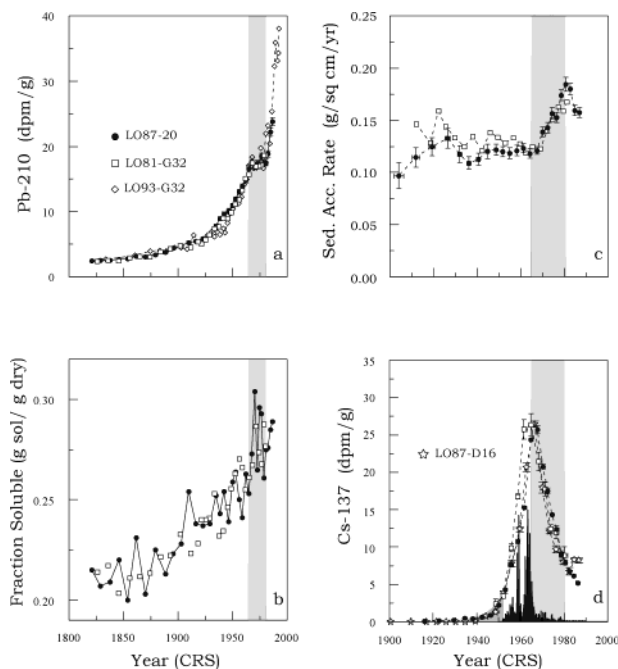


FIGURE 3. Variations of measurements made for sediment sections for years based on the constant rate of ^{210}Pb supply (CRS) dating model. The time period of 1965–1980 associated with the presence of a ^{210}Pb specific activity (SA) plateau is highlighted by shading. (a) ^{210}Pb SA for cores collected within a few kilometers of each other; LO81-G32 in 1981 (44), LO87-20 in 1987 (this study), and LO93-G32 in 1993 (47). (b) Acid peroxide-soluble fractions of sediment solids for the LO 81-G32 and LO87-20 cores. (c) Net sediment accumulation rates determined by CRS. (d) ^{137}Cs SA for the three eastern Lake Ontario cores and LO87-D16. The histogram is the relative monthly deposition of ^{137}Cs over Lake Ontario (74). Small but detectable amounts of ^{137}Cs occur in pre-fallout sediments (shaded area for 1940s).

decline in ^{137}Cs SA proceeds unperturbed through and beyond the ^{210}Pb SA plateau (shaded area) is further evidence against an episode of sediment mixing or slumping between 1965 and 1980. Observed peaks in ^{137}Cs distributions occur at CRS dates of 1965, 1968, and 1966 in cores LO81-G32, LO87-20, and LO87-D16, respectively, and thus are displaced forward from the time of maximum fallout between 1963 and 1964. Such displacements should not be construed as evidence against the validity of the CRS approach since they can result from transport processes that delay deposition of ^{137}Cs in sediments (76).

Variable Rate of Supply (VRS) Analysis. The 50% increase in CRS-determined sediment accumulation rates between 1965 and 1980 is inconsistent with reported changes in concentration of authigenic constituents. In core LO81-G32, Schelske et al. (45) observed a rise of about 2% of sediment mass contributed as BSiO_2 between 1965 and 1980, a rise in CaCO_3 of 3%, and a decrease in organic matter (as CH_2O) of about 3%. In the VRS calculation (see Supporting Information for details), the ^{210}Pb SA plateau is treated as a combined result of increased accumulation of acid peroxide-soluble (authigenic) particles and reduction in the rate of supply of excess ^{210}Pb to sediments (ϕ_e).

Distributions of ^{210}Pb SA in cores LO81-G32 and LO87-20 are shown (Figure 4a) in terms of sediment section ages determined by the VRS method. The VRS model distribution (Figure 4a, solid curve) is the result of a least-squares fit to portions of the distribution in core LO87-20 with ages earlier than 1965. The agreement is excellent and consistent with the profile for LO81-G32. The optimized value of the constant rate of supply of externally loaded materials (primarily clay

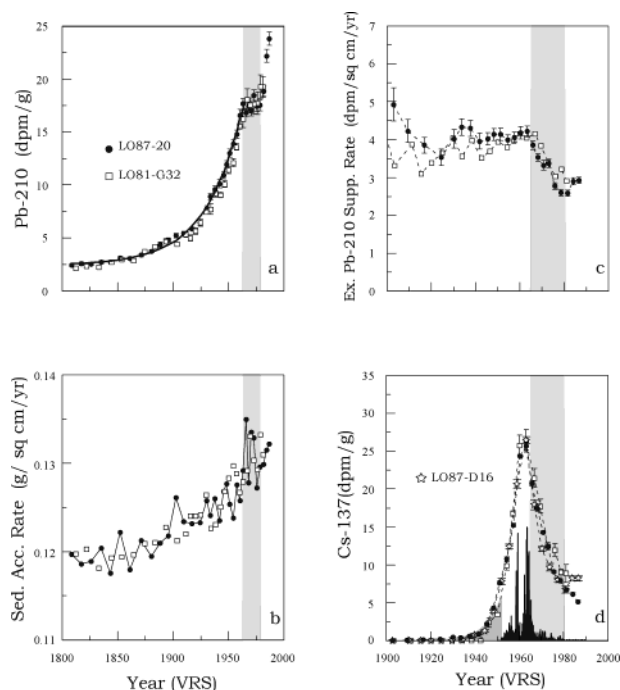


FIGURE 4. Variations of measurements made for sediment sections for years based on the variable rate of ^{210}Pb supply (VRS) dating method. The time period of 1965–1980 associated with the presence of a ^{210}Pb SA plateau is highlighted by shading. (a) ^{210}Pb SA for cores collected within a few kilometers of each other; LO81-G32 in 1981 (44), LO87-20 in 1987 (this study), and LO93-G32 in 1993 (47). The solid line in the VRS model fit to pre-1965 data. (b) VRS determined net sediment accumulation rates. (c) VRS model determined rates of excess ^{210}Pb supply. (d) ^{137}Cs SA for the three eastern Lake Ontario cores and LO87-D16 with respect to the historical ^{137}Cs fallout pattern.

size minerals) (r_e) was $0.094 \text{ g cm}^{-2} \text{ yr}^{-1}$. Thus 70–80% of the VRS model net sediment mass accumulation rate (r_s) is contributed by constant loading of particles from external sources. The relationship between r_s and VRS age for LO87-20 (Figure 4b, filled circles) agrees very well with results for LO81-G32 (Figure 4b, open squares). Note that, within the ^{210}Pb SA plateau (1965–1980) r_s increases only about 6% (from 0.128 to $0.135 \text{ g cm}^{-2} \text{ yr}^{-1}$). The rate of supply of excess ^{210}Pb (ϕ_e) shows a consistent decrease for both cores within the ^{210}Pb SA plateau region (Figure 4c); from 4.0 to $2.6 \text{ dpm cm}^{-2} \text{ yr}^{-1}$ or about a 30% decrease. Thus, VRS mostly attributes the ^{210}Pb SA plateau to a reduction in ϕ_e during the period with highest production of CaCO_3 in the water column. Since nearly twice as much ^{210}Pb accumulates at the site than originates from atmospheric deposition, at least some if not all of it must result from in-lake horizontal redistribution processes. During whiting (calcite precipitation) events in Lake Michigan, the distribution coefficient for ^{210}Pb increases by an order of magnitude, indicating that CaCO_3 can be an efficient scavenger of this radionuclide (72, 77). During periods of intense calcite production in Lake Ontario, patterns of transfer of ^{210}Pb to the lake floor may be altered sufficiently to cause at least temporary reductions in supply to profundal coring sites.

As with the CRS model (Figure 3d), distributions of ^{137}Cs SA in cores LO81-G32, LO87-20, and LO87-D16 in years determined with the VRS model (Figure 4d) are virtually congruent. Peak activities coincide with maximum fallout in spring of 1964.

Resolution of Alternative Age-Depth Relations. Age-depth relations based on CRS and VRS methods are shown in Figure 5a. The small standard deviations shown in

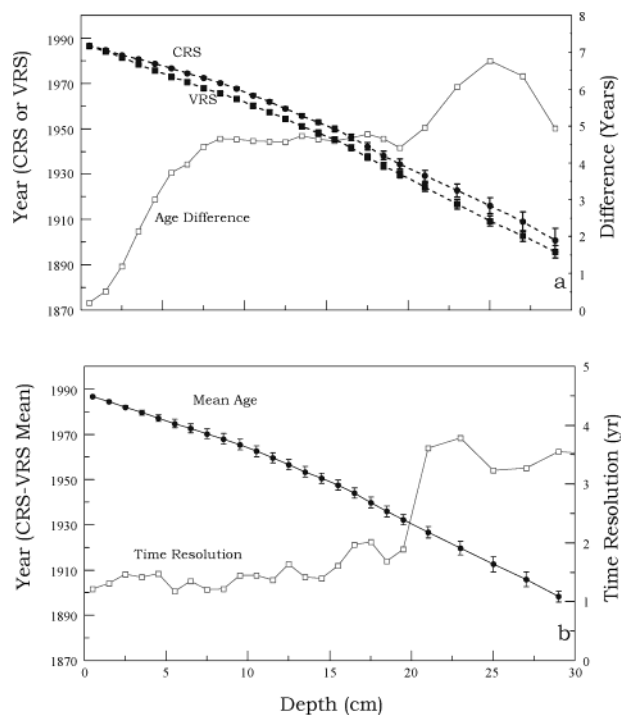


FIGURE 5. Residual dating uncertainties for core LO87-20. (a) Year vs depth from CRS and VRS models with difference with depth (cm) in core. (b) Mean ages assigned to core sections and time resolution based on core section size. The \pm SD bars about the mean dates characterize the uncertainty contributed by differences in ages predicted by the two models.

association with the CRS or VRS dates do not reflect larger variability that would probably be obtained from analysis of replicate LO87-20 cores. Differences between CRS and VRS ages (Figure 5a, open squares) increase with depth from 0 at 1 cm to almost 5 yr at 10 cm and then remain essentially constant for the deeper core sections analyzed for AHR agonists. Although VRS produces generally more consistent results, CRS could be more accurate if there are yet unrecognized sources of nonauthigenic sediment (containing ^{137}Cs) that diluted ^{210}Pb between 1965 and 1980. Without further study, both approaches can be considered viable. Since they represent bounding values from the repertoire of standard interpretive algorithms, means of CRS and VRS ages and standard deviations about these means (Figure 5b) were assigned to sections of cores LO87-20 and LO87-D16 for this study.

The thickness of subcore sections defines the minimum time between events that can be resolved in a sedimentary record. The time resolution is equal to the ratio of subcore section thickness (in g cm^{-2}) to sediment accumulation rate. In core LO87-20, it varies from 1 to 1.5 yr in the upper 20 cm of sediment and is about 3.5 yr below 20 cm where the sediment section thickness changes from 1 to 2 cm (Figure 5b). Note that, without recalculating E subcore section dry weights, mean ages assigned to the E subcores would have underestimated the age of ^{137}Cs maximum by 3 yr in core LO87-20 and overestimated its age by 8 yr in core LO87-D16. Such systematic inter-core differences would have significantly reduced the accuracy of the retrospective lake trout exposure characterization.

Vertical movement of persistent hydrophobic chemicals and associated sediment particles after deposition and burial through processes is expected to be slight. The maximum degree of such movement may be illustrated by distributions of ^{137}Cs because its first delivery to the Great Lakes is known,

1952 (78), and maximum specific activities are about 600 times the typical analytical detection limit of 0.04 dpm/g. Thus slight activities of ^{137}Cs can be measured in sediments with CRS and VRS ages earlier than 1952. As shown by shaded tails on trailing edges of SA distributions (Figures 3d and 4d), ^{137}Cs can be detected up to 6 cm deeper than expected. The observed penetration of slight amounts of ^{137}Cs could be due to translocation during subcoreing rather than diffusion or particle movement. Because the activity of ^{137}Cs redistributed downward is a small part of the total (ca 3%) and diffusion of very hydrophobic organic chemicals is likely to be much less due to very large K_{oc} values, the early record of increasing concentrations of PCDDs, PCDFs, and PCBs in the cores should not be distorted by downward movement of the chemicals in the sediments.

Sediment Core Specific BSAF_{egg}s. Concentrations of PCDDs, PCDFs, and PCBs in 1988 female lake trout whole body and egg samples are reported in Table 1. These data were used to calculate BSAF_{egg}s based on concentrations of these chemicals in the top 1 cm of sediment in core LO87-20 (also Table 1) rather than average concentrations in surface sediment throughout the lake. If calculated on the basis of additional lake trout data (Table 2) from the time periods represented by each core section, BSAFs based on sections 2–3 cm and 5–6 cm of core LO87-20 (ca. 1983 and 1978) are essentially identical to the BSAFs based on section 0–1 cm and 1988 fish. The BSAF_{egg} for TCDD based on core LO87-20 was approximately 3-fold greater than the average BSAF_{egg} determined for 0–1-cm sediment samples collected throughout the sedimentation basins of Lake Ontario (42), whereas the BSAF_{egg} for core LO87-D16 was equal to the average. Since the core-specific BSAF_{egg}s were used to determine changes in Lake Ontario lake trout exposures relative to post-1978 conditions rather than as absolute expressions of a lake-wide average bioaccumulation relationship, systematic differences in magnitudes of BSAF_{egg}s between sites are accommodated. This is consistent with the choice of LO87-20, on the basis of location and greater sedimentation rate, to most accurately represent the decline in exposures of lake trout during the period of 1970 to the present as well as the profile for pre-1970 increases in contamination of Lake Ontario. Similar strategies have been employed for high-resolution measurement of temporal trends in burial of persistent hydrophobic contaminants elsewhere in the Great Lakes (79).

For TCDD and other PCDDs and PCDFs that were detectable in eggs, the ratios of $C_{\text{egg}}/C_{\text{female}}$ were approximately 0.7, although this ratio in PCBs tended to decrease from 0.9 to 0.45 with increasing hydrophobicity or degree of chlorination (Table 1). This trend approximates chemical equilibrium model predictions and is consistent with data for other fish species and ecosystems (80). Because of the relatively small variation in chemical distributions from female lake trout to eggs, female and egg BSAFs similarly range from >10 to 0.3 for PCBs and from 0.27 to <0.001 for PCDDs and PCDFs. The substantial differences in BSAFs between congeners, which are not related to hydrophobicity, are caused by large differences in the rates at which they are metabolized in fish (67). The magnitude of the metabolism-related differences in bioaccumulation of congeners that contribute to risk of lake trout early life stage mortality highlights the benefits of using species, life stage, and site-specific measured BSAFs in the exposure model.

Historical Toxicity Equivalence Record. TEC_{egg}s over time were calculated using eq 4 from cores LO87-20 and LO87-D16 on the basis of contaminant analyses from E subcores and dates determined through radionuclide analyses from G subcores. Determination of when, prior to the 1950s, exposures of lake trout embryos to AHR agonists first caused toxicity is particularly important for development of an

TABLE 1. Concentrations (pg/g wet tissue) of PCDDs, PCDFs, and PCBs in 1988 Lake Ontario Female Lake Trout and Eggs with Associated BSAFs and Ratios of Lipid-Normalized Concentrations in Eggs to Female

chemical	female LT (n = 3)	coeff var (%)	LT eggs (n = 3)	coeff var (%)	L087-20 sediment	female BSAF ^a	egg BSAF ^a	egg/female C _{lipid} ratio
lipid (%)	16.9	23	8.2	4				
2378-TCDD	33.5	27	11.2	43	28.0	0.215	0.148	0.69
2378-TCDF	8.2	25	2.8	47	15.0	0.098	0.070	0.71
12378-PeCDD	4.3	28	1.4	36	4.0	0.193	0.129	0.67
12378PeCDF	1.6	36	0.4		17.0	0.017	0.008	
23478-PeCDF	16.5	26	4.8	78	11.0	0.269	0.162	0.60
123478HxCDD	<2.3 ^b		<1.2		5.1	0.041	0.044	
123678-HxCDD	2.3	43	0.3		21.0	0.020	0.006	
123789-HxCDD	<2.3		<1.2		11.0	0.019	0.020	
123478-HxCDF	3.8	119	1.0		83.0	0.008	0.005	
123678-HxCDF	2.2	106	0.3		22.0	0.018	0.005	
123789-HxCDF	< 0.9		<0.6		8.6	0.009	0.013	
1234678-HpCDD	<2.4		<1.3		338	0.001	0.001	
1234678-HpCDF	<1.0		<0.6		696	0.0001	0.0002	
1234789-HpCDF	<1.0		<0.6		14.0	0.006	0.008	
OCDD	<2.9		2.2		2300	0.0001	0.0002	
OCDF	<2.9		<1.7		2070	0.0001	0.0002	
PCB 28+31	40 700	12	18 200	24	11 400	0.642	0.594	0.92
PCB 52	66 500	30	27 800	42	6 650	1.80	1.55	0.86
PCB 77	3 870	8	1 340	18	1 680	0.413	0.294	0.71
PCB 81	319	13	99.7	27	39	1.47	0.954	0.65
PCB 105	135 000	39	43 600	48	5 860	3.77	2.54	0.67
PCB 118	342 000	34	111 000	49	7 930	7.75	5.22	0.67
PCB 126	2 470	32	731	52	65	6.83	4.18	0.61
PCB 128	40 700	45	17 200	46	680	10.8	9.41	0.87
PCB 138+163	459 000	44	174 000	55	9 360	8.82	6.92	0.78
PCB 156+171+202	60 500	51	16 200	48	1 280	8.50	4.71	0.55
PCB 169	143	39	38.3	60	1.0	12.9	5.58	0.43
PCB 170+190	170 000	50	38 100	55	1 110	27.5	12.8	0.46

^a BSAFs for PCDDs and PCDFs not detected in fish or eggs are based on half of the detection limits. ^b < indicates less than detection limit.

TABLE 2. Concentrations of PCDDs, PCDFs, and PCBs (pg/g wet egg) in Lake Ontario Lake Trout Eggs: 1991–1978

chemical	relative potency	1991	1990	1988	1987 ^a	1984 ^a	1978 ^a
2378-TCDD	1.0	6.03	6.50	11.17	7.26	14.5	25.9
2378-TCDF	0.03	5.83	4.55	2.82	2.93	9.54	18.1
12378-PeCDD	0.73	0.70	<1.3 ^b	1.38	<2.1	2.14	3.53
12378-PeCDF	0.03	2.61	1.30	0.38	0.91	2.62	4.09
23478-PeCDF	0.359	4.60	4.78	4.78	4.65	9.66	18.0
123478-HxCDD	0.32	< 0.8	<1.3	<1.2	<1.1	<0.8	<1.2
123678-HxCDD	0.024	< 0.8	<1.3	0.32	<1.3	1.12	1.81
123789-HxCDD	0.01 ^c	< 0.8	<1.4	<1.2	<1.1	<0.5	<0.5
123478-HxCDF	0.28	1.63	1.80	1.02	1.44	4.36	5.12
123678-HxCDF	0.1 ^c	<0.8	<1.3	0.30	<2.0	<2.2	<3.3
123789-HxCDF	0.01 ^c	<0.8	<1.3	<0.6	<1.8	<0.9	<1.0
1234678-HpCDD	0.002	< 0.8	<1.1	<1.3	0.60	<0.5	0.30
1234678-HpCDF	0.01 ^c	<1.2	<2.2	<0.6	<3.2	0.20	0.20
1234789-HpCDF	0.01 ^c	<1.2	<2.2	<0.6	<3.2	0.90	<0.9
OCDD	<0.0001 ^c	4.00	4.87	2.15	na ^d	na	na
OCDF	<0.0001 ^c	<4.0	<4.0	<1.7	na	na	na
PCB 28+31	na	9 800	na	18 200	na	na	na
PCB 52	na	14900	na	27 800	na	na	na
PCB 77	0.00016	997	1 200	1 340	2 240	2 080	3 850
PCB 81	0.00056	46	na	99.7	na	na	na
PCB 105	<0.000005	12 000	11 700	44 000	56 800	69 000	107 000
PCB 118	<0.000005	39 000	na	111 000	na	na	na
PCB 126	0.005	356	375	731	1 050	1 310	1 430
PCB 128	na	9 200	20	17 200	na	na	na
PCB 138+163	na	94 000	na	174 000	na	na	na
PCB 156+171+202	<0.000005	8 700	na	16 200	na	na	na
PCB 169	0.01	17	na	15	58.70	64.4	48.2
PCB 170+190	na	20 000	na	38 100	na	na	na
TEC _{egg}		10.87	10.96	18.19	15.03	28.00	44.89

^a Concentrations in eggs determined from adult fish using egg/female C_{lipid} ratios from Table 1. ^b < indicates less than detection limit. ^c TEF from ref 70 used, in lieu of a trout relative response factor (RPF) from refs 22 or 24. ^d na indicates not analyzed.

effective model for predicting safe levels of exposure that will not result in sac fry mortality in the future.

Lake trout exposures prior to 1987 were best described by measured concentrations of PCDDs, PCDFs, and PCBs

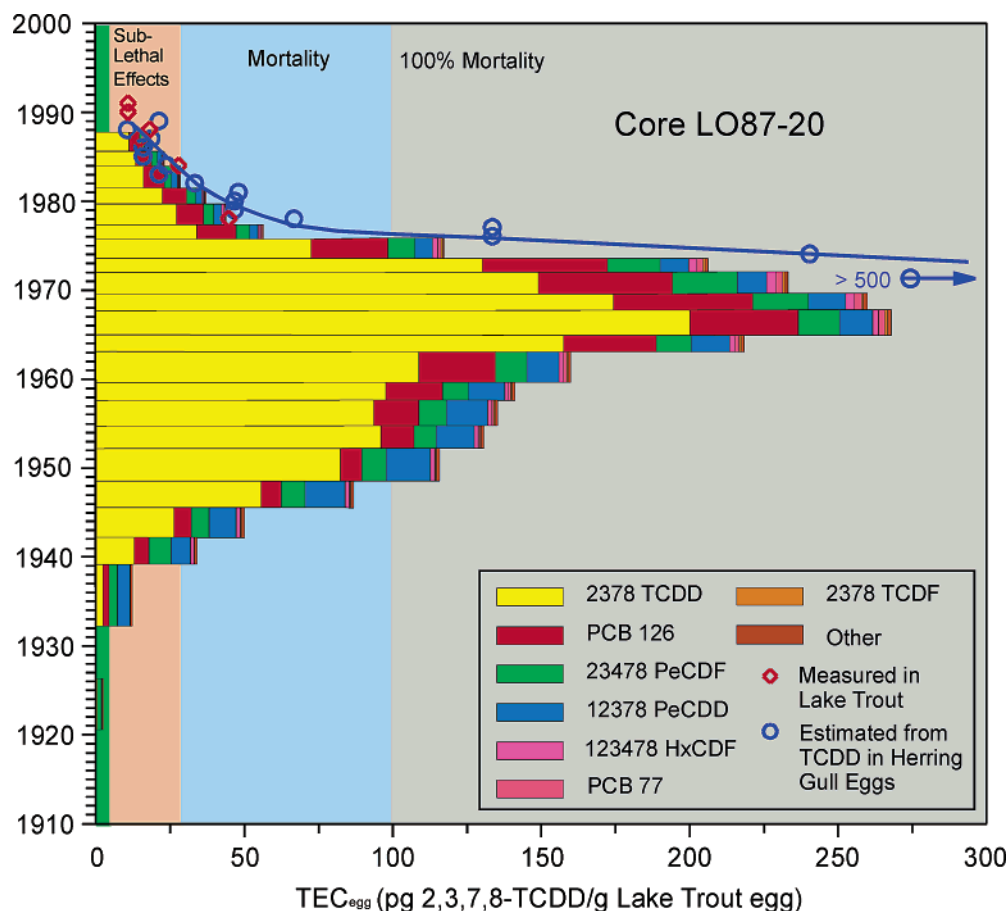


FIGURE 6. Retrospectively determined TEC_{egg} s from analysis of radionuclide-dated 1-cm sections of sediment core LO87-20 in eastern Lake Ontario. The concentrations of each AHR agonist times the appropriate $BSAF_{egg}$ and fish TEF equates to each chemical's contribution to the TEC_{egg} that may be related to mortality expected from acute and chronic toxicity in Lake Ontario lake trout sac fry. Predicted TEC_{egg} s are compared to TEC_{egg} s measured in lake trout and estimated from TCDD concentrations measured in herring gull eggs.

for 21 radionuclide-dated 1-cm sections of the primary reference sediment core from the Rochester Basin of eastern Lake Ontario (LO87-20). Major toxicity equivalence concentrations of the individual PCDD, PCDF, and PCB congeners in lake trout eggs (tec_{egg} s), based on concentrations measured in each section of core LO87-20, are plotted incrementally in Figure 6 with respect to depth in the core, and estimated dates for the sediments in each core section were analyzed. The widths of the horizontal bars vary with respect to the magnitudes of the time periods represented. The length of each horizontal bar in Figure 6 represents the TEC_{egg} (sum of tec_{egg} s). The general pattern of increasing tec_{egg} s (and thus TEC_{egg} s) starting in the 1930s and continuing to maximum concentrations in the late 1960s followed by decreasing concentrations to the present is typical of trends found for PCBs in the Great Lakes through other sediment core analyses. TCDD concentrations appear to peak in about 1967 while PCB concentrations peaked in the period of 1969–1972, which is in agreement with core analyses for PCBs previously reported for Lake Ontario (44, 81, 82). 1,2,3,7,8-Pentachlorodibenzo-*p*-dioxin and 1,2,3,7,8-pentachlorodibenzofuran in Lake Ontario appear to significantly differ from the pattern by reaching high concentrations in the 1940s, which were sustained until the 1970s when they began to decrease as did the other chemicals. The initial appearance of PCDDs and PCDFs and subsequent peak concentrations are both significantly earlier in LO87-20 than the core profiles reported for a series of fluorinated compounds that are associated with TCDD at a landfill operated between 1953 and 1975 near the Niagara River (83). Concentrations of TCDD in anaerobic sediments are unlikely to have been increased

through selective dechlorination of PCDDs with greater chlorination (84). The appearance of PCDDs and PCDFs in the reference core prior to 1940 and the large concentrations reached during the 1940s indicate that other sources of these chemicals, probably with different congener mixtures, contributed to lake trout exposures prior to 1953. The magnitude of TEC_{egg} s and the temporal pattern of the chemical mixture determined from core LO87-D16 (Figure 7) is very similar to those determined from LO87-20 (Figure 6).

Maximum TEC_{egg} s were calculated by adding maximum possible toxicity contributions from mono-ortho-chlorinated biphenyl congeners. RPFs for these congeners were based on the greatest no effect doses studied to date for trout early life stage mortality (24). Maximum TEC_{egg} s were always less than 105% of the minimum lake trout TEC_{egg} s, which were calculated only for AHR agonists with measured lethality to trout sac fry. Thus, the minimum TEC_{egg} s plotted in Figures 6 and 7 do not account for additional toxicity from chemicals that presently do not have measured potencies for trout early life stage mortality. Lake Ontario is unusual, relative to the other Great Lakes, in that TCDD contributes approximately 60% of the predicted TEC_{egg} . TEC_{egg} s in Lake Michigan lake trout are largely related to PCBs and PCDFs with TCDD's contribution only 12% (85). Only six PCDD, PCDF, and PCB congeners other than TCDD contributed more than 1% each to the Lake Ontario TEC_{egg} . While predicted TEC_{egg} s are less than the 30 pg TCDD/g egg threshold concentration for lake trout sac fry mortality after 1984, exposures are predicted to have resulted in direct mortality under lake conditions from the late-1930s to mid-1980s, with 100% mortality from about 1948 to 1976 (Figure 6).

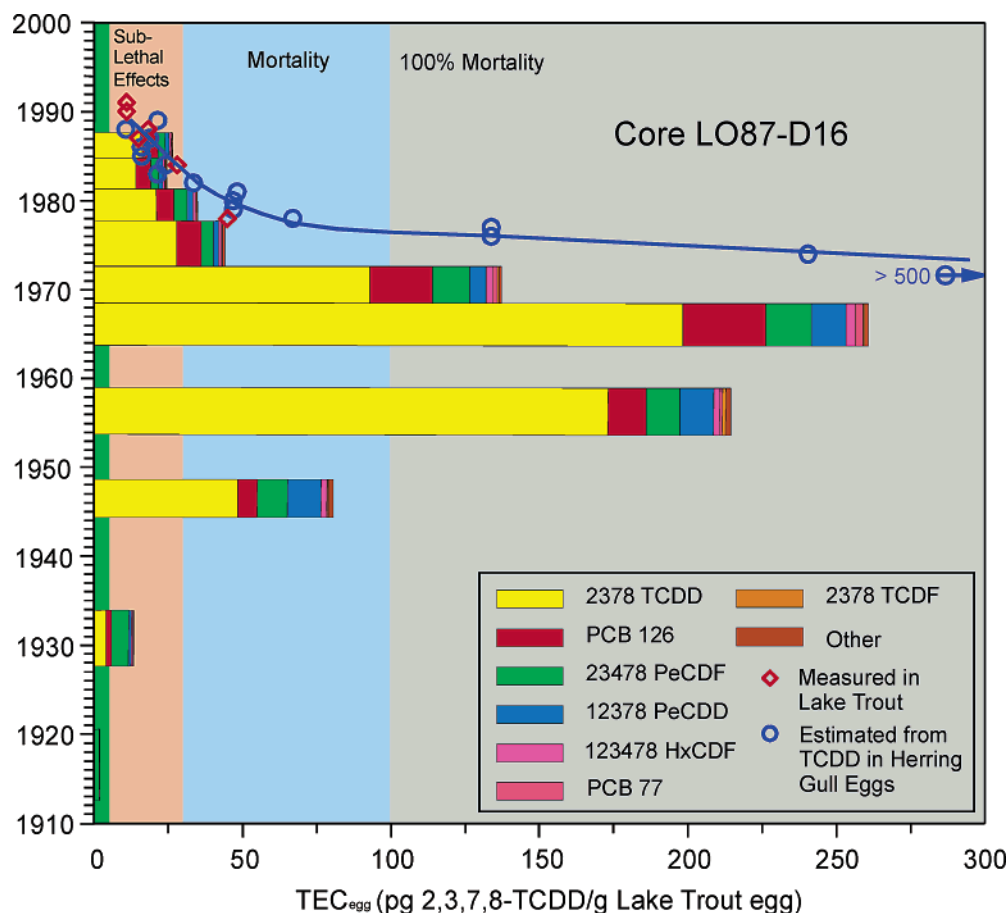


FIGURE 7. Retrospectively determined TEC_{egg} s from analysis of radionuclide-dated 1-cm sections of sediment core LO87-D16 in south central Lake Ontario. The concentrations of each AHR agonist times the appropriate $BSAF_{egg}$ and fish TEF equates to each chemical's contribution to the TEC_{egg} that may be related to mortality expected from acute and chronic toxicity in Lake Ontario lake trout sac fry. Predicted TEC_{egg} s are compared to TEC_{egg} s measured in lake trout and estimated from TCDD concentrations measured in herring gull eggs.

Direct analysis of past TEC_{egg} s for Lake Ontario lake trout was restricted to egg samples from 1991, 1990, and 1988 (Table 2). On the basis of the egg/female chemical concentration ratios reported in Table 1, TEC_{egg} s were estimated as 0.33 times TEC_{adult} for whole lake trout from 1987, 1984, and 1978 (Table 2). The observed agreement between predicted and measured TEC_{egg} s is limited to the period of 1978–1991 because adult lake trout with eggs were not present from the early-1950s until 1978. In an attempt to validate TEC_{egg} predictions further back in time when the lake trout was absent in Lake Ontario, concentrations of TCDD in lake trout eggs [measured or estimated from adult fish for years 1988, 1987, 1984, and 1978 (Table 2)] were correlated to the contemporaneous concentrations of TCDD in herring gull eggs from Scotch Bonnet Island in eastern Lake Ontario (86). The lake trout egg/gull egg TCDD concentration ratio (0.16 wet wt basis) was then used to predict concentrations of TCDD and the other chemicals contributing to TEC_{egg} s for lake trout back to 1970 on the basis of the herring gull egg data (Figures 6 and 7). Good agreement was found between measured TCDD concentrations in lake trout eggs, predictions based on herring gull egg data, and the $BSAF_{egg}$ predictions of C_{egg} for the period in which lake trout samples were analyzed. However, for the earlier period of 1971–1977, when TCDD concentrations in herring gull eggs were probably rapidly declining from maximum values reached in the 1960s, the lake trout/gull egg TCDD ratio when applied to the herring gull egg data predict TCDD concentrations in lake trout eggs (and thus TEC_{egg} s), which are 2–3 times greater than predicted by the $BSAF$ model. This difference prior to 1978 may be caused by a true divergence of the ratio of TCDD

likely in lake trout eggs (if adult lake trout had been present) and herring gull eggs. Such a divergence would be expected if the herring gull's diet was primarily near shore fish without deep benthic food chain connections. Alternatively, underestimation of the impact of change in Π_{socw} on the lake trout $BSAF_{egg}$ relevant to that time could cause underestimation of the predicted TEC_{egg} s for lake trout. Without the $BSAF_{egg}$ adjustments for historical changes in Π_{socw} made for this assessment, the divergence of the herring gull data and predicted lake trout egg TCDD concentrations for the 1970s would be greater.

Discussion

The predicted lake trout TEC_{egg} s shown in Figures 6 and 7 indicate a 40-yr period during which TCDD toxicity-associated mortality of sac fry would adversely impact the population, regardless of effects caused by other stressors, either chemical or nonchemical. The plausibility of these risk predictions rests with the degree to which they are supported by independent exposure and effects information as well as epidemiological data.

Limited data exist for the incidence of mortality of sac fry hatched from eggs of feral lake trout from Lake Ontario. Eggs collected in 1991 did not produce sac fry with observable blue sac syndrome or increased mortality as compared to controls (31). However, when the 1991 eggs were exposed to TCDD through injection, the LC_{egg50} was 47 pg TCDD/g egg (31). The apparent reduction of the LC_{egg50} from the expected average of 60–65 pg TCDD/g egg is consistent with the incremental contribution of 11 pg TCDD equivalence/g egg,

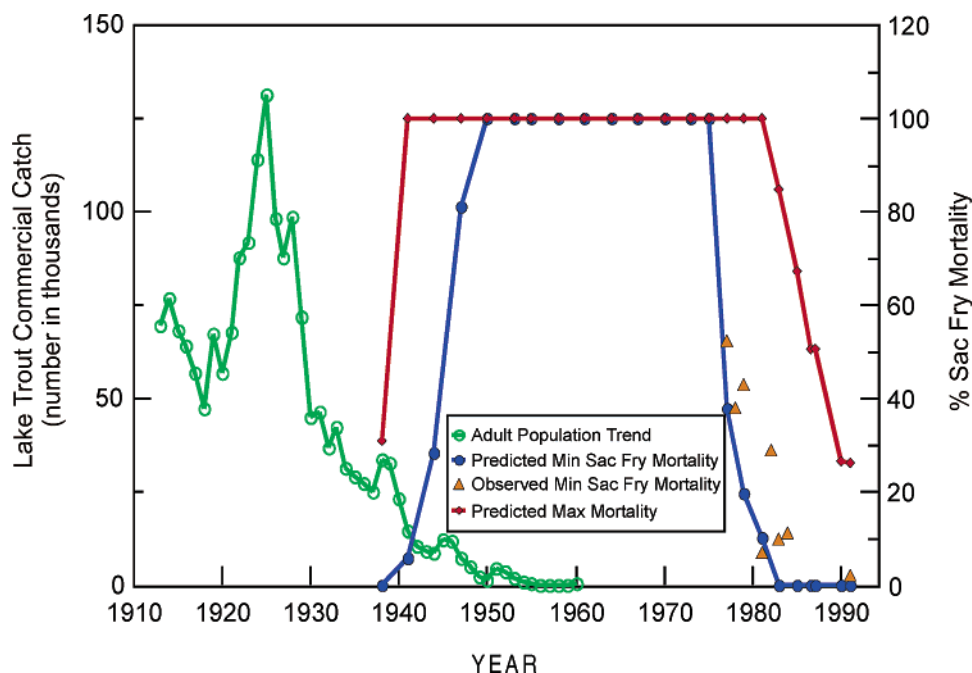


FIGURE 8. Integrated sediment core analysis and toxicity model predicted lake trout sac fry mortality (acute and chronic toxicity related) in comparison to lake trout population decline prior to extirpation around 1960 and blue sac syndrome mortality observed for sac fry raised from fertilized eggs collected from stocked fish between 1976 and 1990.

which was measured in the feral eggs. Mortality associated with signs of toxicity that resembled blue sac disease was observed for sac fry hatched from eggs collected from Lake Ontario lake trout during the period of 1977–1984 (27, 87). Mean percent mortality, above control, of sac fry with blue sac disease in 1977, 1978, 1979, 1981, 1983, and 1984 (data kindly provided by H. Simonin, New York Department of Environmental Conservation) tended to slightly exceed the minimum TCDD toxicity equivalence model predictions (Figure 8).

The observations of Lake Ontario lake trout sac fry mortality occurred during the period in which concentrations of PCDDs, PCDFs, and PCBs in lake trout eggs were measured directly or estimated from females (Table 2). The sac fry mortality incidence data agree well with toxicity predictions based on TEC_{eggs} measured for the period 1978–1991. The model predictions are also consistent with egg exposures estimated from annual mean PCDD and PCDF concentrations in adult lake trout reported (88) for the period 1977–1993 when adjusted for egg/female lipid-normalized concentration ratios reported in Table 1. Any underestimation of lake trout sac fry mortality during this period of declining risk is probably not caused by an underestimation of maternal exposures to the congeners listed in Table 2. The exposure model does not account for increases in chemical concentrations in freshly fertilized eggs deposited on spawning reefs that might result through accumulation of the chemicals from water and sediment. Additive trout early life stage toxicity equivalence has been demonstrated for binary combinations of AHR agonists (33). TEC_{eggs} for graded doses of a mixture of 14 PCDDs, PCDFs, and PCBs, which simulated the mixture of known AHR agonists measured in Lake Michigan lake trout eggs in 1994, accurately predicted lake trout sac fry mortality (32). Thus, use of the additive toxicity equivalence model for complex mixtures of AHR agonists is supported. Greater than additive or synergistic contributions of the chemicals measured in Lake Ontario lake trout eggs seem unlikely. It is possible that Lake Ontario lake trout are exposed to and bioaccumulate other AHR agonists, such as polybrominated dibenzo-*p*-dioxins, dibenzofurans, and biphenyls for which trout embryo relative potencies have been

measured (89). Although such chemicals were not included in this assessment, they could add to lake trout TEC_{eggs} and thus risk.

The lack of evidence for adult lake trout mortality associated with AHR-mediated toxicity during the period after 1973, when an adult population was re-established in Lake Ontario through annual stocking of yearlings, is consistent with studies of the toxicity of TCDD and related chemicals to different life stages of salmonids. Female lake trout, with dietary exposures to TCDD more than three times greater than those which resulted in 100% sac fry mortality, appeared to fail to ovulate and had nonviable oocytes while exhibiting no overt signs of toxicity (30). Adult brook trout grew and spawned successfully (90) at dietary exposure levels of TCDD that resulted in 100% mortality of their progeny (68). No effect of TCDD on fecundity was observed although exposure of female brook trout was relatively late during oogenesis (90). It is uncertain whether improved fecundity of individual adult female lake trout contributed to the estimated (91) 8-fold increase in fecundity of the Lake Ontario lake trout population between 1980 and 1994. Given the association during this time period between improved signs of natural reproduction, declining TEC_{eggs} , and increased fecundity of the Lake Ontario lake trout population, investigation of the effects from long-term exposures to TCDD on fecundity is warranted.

Sublethal toxicity effects, combined with effects from or interactions with other stressors in Lake Ontario, become a greater concern after the mid-1980s. In Figure 8, the historical native lake trout population trends, as has been reported on the basis of reliable commercial catch records (92), are compared to two early life stage mortality risk curves. One is based on minimum expected lake trout early life stage mortality as directly predicted from TCDD-induced mortality in laboratory studies. The second risk curve is a simulation of hypothetical maximum lake trout early life stage mortality attributable to all AHR-mediated toxicity effects under actual environmental conditions. The maximum risk simulation assumes that survival of sac fry or alevins under environmental conditions is reduced in comparison to survival under laboratory conditions because sublethal effects can increase

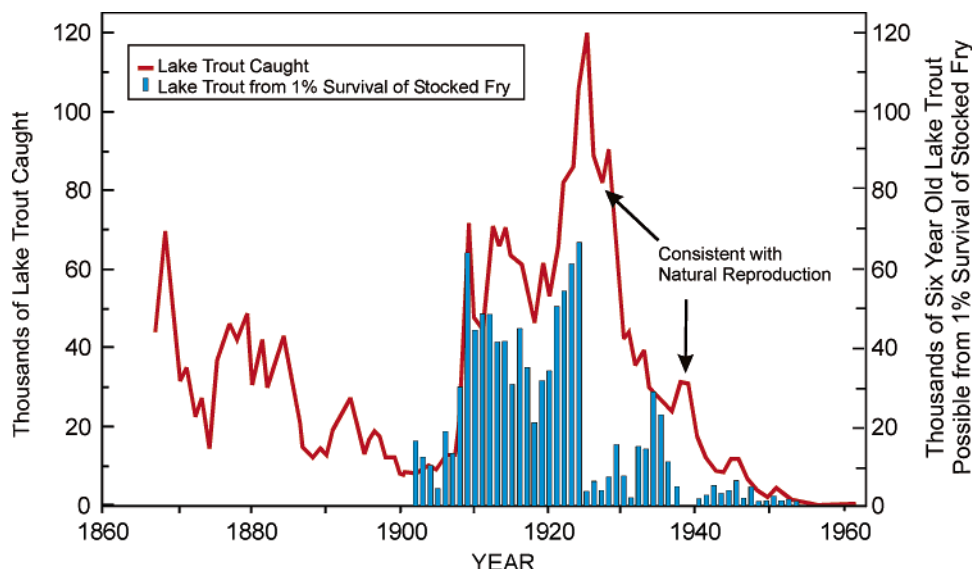


FIGURE 9. Association of lake trout population levels, as revealed by commercial catch (thousands) prior to 1940, with numbers of 6-year-old lake trout (thousands) from hypothetical survival of 1% of fry stocked into Lake Ontario.

susceptibility to predation and mortality during critical events such as swim-up. Some observations support this hypothesis. Poorer sac fry survival from in situ incubation of Lake Ontario lake trout eggs than for eggs incubated in the laboratory (11% vs 69%) was attributed to stress from warmer water temperatures at spawning in the lake (10). Sublethal effects observed in trout sac fry survivors in TCDD toxicity studies include skeletal malformations (68, 93), reductions in growth (94), and reduced energy for feeding (94). Reduced heart size and impaired blood flow, although only examined in trout sac fry that were likely to die from TCDD induced toxicity (93), may indicate related cardiovascular dysfunction at sublethal exposures. Sublethal exposures of rainbow trout embryos to TCDD result in decreased retinal ganglion density and deficits in visual function following fry swim-up when the ability to capture prey and avoid predators is paramount for survival (95). Ecological concerns at sublethal levels of TCDD exposure for which there are no laboratory data available include the capability to avoid predation at different stages or pass critical developmental steps such as swim-up to inflate the gas bladder (96) or initiation of feeding under environmental conditions. With these considerations, the second risk curve is based on 100% sac fry mortality at a TEC_{egg} of 50 pg/g egg and a threshold for toxicity related mortality at 5 pg/g egg. Choice of the threshold TEC_{egg} of 5 pg/g egg rests on an assumption that this level of exposure, probably experienced by Lake Superior lake trout during the 1960s and 1970s, was not associated with the observed reduction in the numbers of native lake trout during the same time period (97).

From Figure 8, one may ask why the dramatic decline in the Lake Ontario lake trout population began in the 1930s instead of the 1940s when toxicity risks are predicted to become great. It appears that the Lake Ontario lake trout population was probably supported for a long period by the stocking of fry in U.S. waters. The decline in fry stocking in the 1920s, documented by Elrod et al. (4), resulted in fewer adult fish to catch in the 1930s. An association between numbers of lake trout removed through commercial harvest and numbers of fry stocked during the period of 1896–1947 is apparent (4). This association appears more remarkable when the fry stocking pattern is shifted 7 yr forward to project its potential impact on numbers of adult lake trout available for the commercial harvest (Figure 9). This association, illustratively based on an approximation of 1% survival of stocked fry to harvest, suggests that the rate of survival of

stocked fry was good. A final observation, very relevant to this assessment, is the appearance of natural reproduction from the adult lake trout that originated as stocked fry. Although numbers of adult lake trout caught eventually declined in response to abrupt decreases in fry stocking around 1918 and 1930, the declines appear to have been delayed or reduced due to availability of lake trout both from the earlier fry stocking and subsequently from their progeny. The approximate periods of 1925–1932 and 1936–1940 are most suggestive of this effect. The presence during these periods of second generation adult trout, from fry which were stocked approximately 14 yr earlier, indicates that natural reproduction and fry survival was good at least until the mid-1930s. This would be consistent with the toxicity risk predictions made in this paper.

Much of the uncertainty for this retrospective assessment involved prediction of exposure and bioaccumulation for years when egg samples were not available for analysis or when lake trout were absent from the ecosystem. This uncertainty was reduced through use of the sediment contamination record and BSAFs to reconstruct TEC_{eggs} , which were then validated with bioaccumulation data from the period after 1970. Uncertainty for prediction of direct early life stage mortality is small because of the very precise, reproducible determinations of embryo TCDD dose–response data. Less certain are recent and future ecological risks associated with potential adverse effects in young lake trout when TEC_{eggs} are less than the threshold for TCDD toxicity-associated sac fry mortality. TEC_{eggs} of <3 pg/g egg in ecosystems having lake trout populations with good reproduction and recruitment provide a lower bound for toxicity risks. With TEC_{eggs} now below 10 pg/g egg, there is uncertainty for the magnitude of present AHR-mediated toxicity risks to survival of lake trout during early life stage development in Lake Ontario. However, since the mid-1980s there has been a slow but consistent movement of the species toward a condition under which natural reproduction can begin to support the population and its dependence on stocking reduced. Further reduction in AHR-mediated toxicity risk will occur in parallel with declines in concentrations of PCDDs, PCDFs, and PCBs in the surficial sediments because of the lake trout's exposure through the benthic food chain. This assumes that new loadings of persistent bioaccumulative chemicals with AHR-mediated toxicity potential will not occur.

The chemical mixture, residue-based, early life stage toxicity approach used in this risk assessment is applicable to other species and problems. For example, in eastern Lake Ontario the TEC_{egg} associated with herring gull reproductive failure observed in the 1970s (98) is about 2000 pg/g egg, based on herring gull egg BSAFs and avian TEFs (70). In contrast to the strong impact of TCDD on the lake trout, avian TEFs allocate a much greater contribution from PCBs to overall AHR-mediated toxicity risks for the gulls. Consistent with the observed relative insensitivity of herring gulls, their reproduction was restored around 1975. On the basis of this observation and the temporal profile of PCDD, PCDF, and PCB concentrations in Lake Ontario, the reference sediment cores indicate that the herring gull reproductive problem probably began around 1960, long after the lake trout population declined.

Acknowledgments

Special thanks to Anthony Kizlauskas of U.S. EPA Region 5 for supporting the collection of sediment cores in 1987 for historical analysis in conjunction with EPA's Lake Ontario TCDD Bioaccumulation Study. We gratefully acknowledge the captain and crew of the U.S. Environmental Protection Agency R/V *Roger Simons* and M. Brake, Cooperative Institute for Limnological and Environmental Research (CILER), for help in the collection of sediment cores. Thanks are due N. Morehead (Great Lakes Environmental Research Laboratory, NOAA) for help in core sample processing and dating analysis. This assessment would not have been possible without the excellent chemical analyses, coordinated by Brian Butterworth and provided by Philip Marquis, Chris Berini, John Libal, David Marklund, Sarah Grosshuesch, and Chris Harper. We are indebted to Roger LePage of CSC Corp. for color graphics assistance. U.S. EPA Office of Research and Development grants to the University of Minnesota—Duluth for exposure assessment research and the University of Wisconsin for toxicology research, conducted in concert with research supported by the University of Wisconsin Sea Grant Institute under grants from the National Sea Grant College Program, were instrumental in providing much of the data and models. Very helpful reviews were provided by Gerald Ankley and Tala Henry of U.S. EPA. Finally, our appreciation is extended to the many researchers and administrators, especially in the Great Lakes community, who provided insights, ancillary data, and advice during the decade over which this research has been in progress. This report has been reviewed by the U.S. EPA National Health and Environmental Effects Research Laboratory and approved for publication. Approval does not signify that the contents reflect the views of the Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

Supporting Information Available

Details of methods used for chemical analyses of fish, egg, and sediment samples and radionuclide dating of sediments. This material is available free of charge via the Internet at <http://pubs.acs.org>.

Literature Cited

- Christie, W. J. *J. Fish. Res. Board Can.* **1972**, *29*, 913–929.
- Christie, W. J. *J. Fish. Res. Board Can.* **1974**, *31*, 827–854.
- Hartman, W. L. *Adv. Environ. Sci. Technol.* **1988**, *21*, 103–131.
- Elrod, J. H.; O'Gorman, R.; Schneider, C. P.; Eckert, T. H.; Schaner, T.; Bowlby, J. N.; Schleen, L. P. *J. Great Lakes Res.* **1995**, *21* (Suppl. 1), 83–107.
- Marsden, J. E.; Krueger, C. C.; Schneider, C. P. *J. Great Lakes Res.* **1988**, *14*, 3–8.
- Schneider, C. P.; Eckert, T. H.; Elrod, J. H.; O'Gorman, R.; Owens, R. W.; Schaner, T. *1995 Annual Report Bureau of Fisheries Lake Ontario Unit to the Lake Ontario Committee and the Great Lakes Fishery Commission*; New York State Department of Environmental Conservation: Cape Vincent, NY, 1995; Section 7, pp 1–4.
- Lantry, B. F.; Eckert, T. H.; O'Gorman, R.; Owens, R. W. In *2000 Annual Report—Bureau of Fisheries Lake Ontario Unit and St. Lawrence River Unit to the Great Lakes Fishery Commission's Lake Ontario Committee*; New York State Department of Environmental Conservation: Cape Vincent, NY, 2001; Section 5, pp 1–10.
- Sly, P. G. *J. Great Lakes Res.* **1988**, *14*, 301–315.
- Burnham-Curtis, M. K.; Krueger, C. C.; Schreiner, D. R.; Johnson, J. E.; Stewart, T. J.; Horrall, R. M.; MacCallum, W. R.; Kenyon, R.; Lange, R. E. *J. Great Lakes Res.* **1995**, *21* (Suppl. 1), 477–486.
- Casselman, J. M. *J. Great Lakes Res.* **1995**, *21* (Suppl. 1), 384–399.
- Krueger, C. C.; Perkins, D. L.; Mills, E. L.; Marsden, J. E. *J. Great Lakes Res.* **1995**, *21* (Suppl. 1), 458–469.
- Mac, M. J.; Edsall, C. C. *J. Toxicol. Environ. Health* **1991**, *33*, 375–394.
- Oliver, B. G.; Charlton, M. N.; Durham, R. W. *Environ. Sci. Technol.* **1989**, *23*, 200–208.
- Zacharewski, T. L.; Safe, L.; Safe, S.; Chitum, B.; DeVault, D.; Wiberg, K.; Berquist, P. A.; Rappe, C. *Environ. Sci. Technol.* **1989**, *23*, 730–735.
- DeVault, D. S.; Hesselburg, R.; Rogers, P. W.; Feist, T. J. *J. Great Lakes Res.* **1996**, *22*, 884–895.
- Kirilik, R. M.; Servos, M. R.; Whittle, D. M.; Cabana, G.; Rasmussen, J. B. *Can. J. Fish. Aquat. Sci.* **1995**, *52*, 2660–2674.
- Cook, P. M.; Kuehl, D. W.; Walker, M. K.; Peterson, R. E. In *Biological Basis for Risk Assessment of Dioxins and Related Compounds*; Gallo, M. A., Scheuplein, R. J., Van der Heijden, K. A., Eds.; Banbury Report 35; Cold Spring Harbor Press: Plainview, NY, 1991; pp 143–167.
- Poland, A.; Knutson, J. C. *Annu. Rev. Pharmacol. Toxicol.* **1982**, *22*, 517–554.
- Hahn, M. E.; Poland, A.; Glover, E.; Stegeman, J. J. *Arch. Biochem. Biophys.* **1994**, *310*, 218–228.
- Hahn, M. E. Evolutionary and physiological perspectives on Ah receptor function and dioxin toxicity. In *Dioxins and Health*, 2nd ed.; Schecter, A., Gasiewicz, T. A., Eds.; Wiley: New York, 2003; pp 559–602.
- Tanguay, R. L.; Andreasen, E. A.; Walker, M. K.; Peterson, R. E. Dioxin toxicity and aryl hydrocarbon receptor signaling in fish. In *Dioxins and Health*, 2nd ed.; Schecter, A., Gasiewicz, T. A., Eds.; Wiley: New York, 2003; pp 603–628.
- Walker, M. K.; Peterson, R. E. *Aquat. Toxicol.* **1991**, *21*, 219–238.
- Zabel, E. W.; Cook, P. M.; Peterson, R. E. *Environ. Toxicol. Chem.* **1995**, *14*, 2175–2179.
- Zabel, E. W.; Cook, P. M.; Peterson, R. E. *Aquat. Toxicol.* **1995**, *31*, 315–328.
- Guiney, P. D.; Smolowitz, R. M.; Peterson, R. E.; Stegeman, J. J. *Toxicol. Appl. Pharmacol.* **1997**, *143*, 256–273.
- Wolf, K. *Prog. Fish-Cult.* **1957**, *19*, 14–18.
- Symula, J.; Meade, J.; Skea, J. C.; Cummings, L.; Colquhoun, J. R.; Dean, H. J.; Miccoli, J. *J. Great Lakes Res.* **1990**, *16*, 41–52.
- Spitsbergen, J. M.; Walker, M. K.; Olson, J. R.; Peterson, R. E. *Aquat. Toxicol.* **1991**, *19*, 41–72.
- Walker, M. K.; Spitsbergen, J. M.; Olson, J. R.; Peterson, R. E. *Can. J. Fish. Aquat. Sci.* **1991**, *48*, 875–883.
- Walker, M. K.; Cook, P. M.; Batterman, A. R.; Butterworth, B. C.; Berini, C.; Hufnagle, L.; Peterson, R. E. *Can. J. Fish. Aquat. Sci.* **1994**, *51*, 1410–1419.
- Guiney, P. D.; Cook, P. M.; Casselman, J. M.; Fitzsimons, J. D.; Simonin, H. A.; Zabel, E. W.; Peterson, R. E. *Can. J. Fish. Aquat. Sci.* **1996**, *53*, 2080–2092.
- Walker, M. K.; Cook, P. M.; Butterworth, B. C.; Zabel, E. W.; Peterson, R. E. *Fundam. Appl. Toxicol.* **1996**, *30*, 178–186.
- Zabel, E. W.; Walker, M. K.; Hornung, M. W.; Clayton, M. K.; Peterson, R. E. *Toxicol. Appl. Pharmacol.* **1995c**, *134*, 204–213.
- Fitzsimons, J. D.; Vandenbyllaardt, L.; Brown, S. B. *Aquat. Toxicol.* **2001**, *52*, 29–239.
- Mac, M. J.; Schwartz, T. R.; Edsall, C. C.; Frank, A. M. *J. Great Lakes Res.* **1993**, *19*, 752–765.
- Fitzsimons, J. D. *J. Great Lakes Res.* **1995**, *21* (Suppl. 1), 277–285.
- Edwards, C. J.; Ryder, R. A.; Marshall, T. R. *J. Great Lakes Res.* **1990**, *16*, 591–608.
- Parent, S.; Schriml, L. M. *Can. J. Fish. Aquat. Sci.* **1995**, *52*, 1768–1781.
- Elonen, G. E.; Spehar, R. L.; Holcombe, G. W.; Johnson, R. D.; Fernandez, J. D.; Erickson, R. J.; Tietge, J. E.; Cook, P. M. *Environ. Toxicol. Chem.* **1998**, *17*, 472–483.

- (40) Fitzsimons, J. D. *J. Great Lakes Res.* **1995**, *21* (Suppl. 1), 267–276.
- (41) Barnthouse, L. W.; Glaser, D.; Young, J. *Environ. Sci. Technol.* **2003**, *37*, 229–234.
- (42) U.S. EPA. *Lake Ontario TCDD Bioaccumulation Study*, 1990 (copies available from P.M.C.).
- (43) Kemp, A. L. W.; Harper, N. S. *J. Great Lakes Res.* **1976**, *2*, 324–340.
- (44) Eisenreich, S. J.; Capel, P. D.; Robbins, J. A.; Bourbonniere, R. *Environ. Sci. Technol.* **1989**, *23*, 1116–1126.
- (45) Schelske, C. L.; Robbins, J. A.; Gardner, W. S.; Conley, D. J.; Bourbonniere, R. A. *Can. J. Fish. Aquat. Sci.* **1988**, *45*, 129–1303.
- (46) Pearson, R. F.; Swackhammer, D. L.; Eisenreich, S. J.; Long, D. T. *Environ. Sci. Technol.* **1997**, *31*, 2903–2909.
- (47) Hodell, D. A.; Schelske, C. L.; Fahnenstiel, G. L.; Robbins, L. L. *Limnol. Oceanogr.* **1998**, *43*, 187–199.
- (48) Kuehl, D. W.; Butterworth, B. C.; Libal, J.; Marquis, P. J. *Chemosphere* **1991**, *22*, 849–858.
- (49) Marquis, P. J.; Hackett, M.; Holland, L. G.; Larsen, M. L.; Butterworth, B.; Kuehl, D. W. *Chemosphere* **1994**, *29*, 495–508.
- (50) Swackhamer, D. L. *Quality assurance plan, Green Bay mass balance study. 1: PCBs and dieldrin*; Prepared by University of Minnesota for U.S. EPA, Great Lakes National Program Office: 1988; 22 pp.
- (51) Flynn, W. W. *Anal. Chim. Acta* **1968**, *43*, 221–227.
- (52) Goldberg, E. D. *Radioactive Dating*; International Atomic Energy Agency: Vienna, Austria, 1963; pp 121–131.
- (53) Krishnaswami, S.; Lal, D.; Martin, J. M.; Meybeck, M. *Sci. Lett.* **1971**, *11*, 407–414.
- (54) Robbins, J. A.; Edgington, D. N. *The use of natural and fallout radionuclides to measure recent sedimentation rates in southern Lake Michigan*; Radiological and Environmental Research Division Annual Report, ANL-7960, Part III.; Argonne National Laboratory: Argonne, IL, 1972.
- (55) Robbins, J. A.; Edgington, D. N. *Geochim. Cosmochim. Acta* **1975**, *38*, 285–304.
- (56) Robbins, J. A. In *Biogeochemistry of Lead in the Environment, Part A*; Nriagu, J. O., Ed.; Elsevier Scientific Publishers: Amsterdam, 1978; Vol. 1A, pp 285–393.
- (57) Appleby P. G.; Oldfield, F. *Catena* **1978**, *5*, 1–8.
- (58) Robbins, J. A.; Herche, L. R. *Verh. Int. Ver. Limnol.* **1993**, *25*, 217–222.
- (59) U.S. EPA. *Guidelines for ecological risk assessment*; EPA/630/R-95/002F; U.S. Government Printing Office: Washington, DC, 1998.
- (60) U.S. EPA. *Workshop report on the application of 2,3,7,8-TCDD toxicity equivalence factors to fish and wildlife*; EPA/630/R-01/002; U.S. Government Printing Office: Washington, DC, 2001.
- (61) Ankley, G. T.; Cook, P. M.; Carlson, A. R.; Call, D. J.; Swenson, J. A.; Corcoran, H. F.; Hoke, R. A. *Can. J. Fish. Aquat. Sci.* **1992**, *49*, 2080–2085.
- (62) Thomann, R. V.; Connolly, J. P.; Parkerton, T. F. *Environ. Toxicol. Chem.* **1992**, *11*, 615–629.
- (63) Cook, P. M.; Burkhard, L. P. In *Proceedings of the National Sediment Bioaccumulation Conference*; EPA 823-R-98-002; U.S. EPA Office of Water: Washington, DC, 1996; pp 3–19–3–27.
- (64) Burkhard, L. P.; Cook, P. M.; Mount, D. R. *Environ. Toxicol. Chem.* (in press).
- (65) Gobas, F. A. P. C.; Z'Graggen, M. N.; Zhang, X. *Environ. Sci. Technol.* **1995**, *29*, 2038–2046.
- (66) Oliver, B. G.; Niimi, A. J. *Environ. Sci. Technol.* **1988**, *22*, 388–397.
- (67) Endicott, D. D.; Cook, P. M. *Chemosphere* **1994**, *28*, 75–87.
- (68) Johnson, R.; Tietge, J.; Jensen, K.; Fernandez, J.; Lothenbach, D.; Holcombe, G.; Cook, P.; Drummond, R. *Environ. Toxicol. Chem.* **1998**, *17*, 2408–2421.
- (69) Safe, S. *Crit. Rev. Toxicol.* **1990**, *21*, 51–88.
- (70) Van den Berg, M.; Birnbaum, L.; Bosveld, B. T. C.; Brunstrom, B.; Cook, P. M.; Feeley, M.; Giesy, J. P.; Hanberg, A.; Hasegawa, R.; Kennedy, S. W.; Kubiak, T.; Larsen, J. C.; van Leewen, F. X. R.; Dijen Liem, A. K.; Nolt, C.; Peterson, R. E.; Poellinger, R. E.; Safe, S.; Schrenk, D.; Tillitt, D.; Tysklind, M.; Waern, F.; Zacherewski, T. *Environ. Health Perspect.* **1998**, *106*, 775–792.
- (71) Hawley, N. J.; Robbins, J. A.; Eadie, B. J. *Geochim. Cosmochim. Acta* **1987**, *50*, 1127–1131.
- (72) Eadie, B. J.; Robbins, J. A. In *Sources and Fates of Aquatic Pollutants*; Hites, R. A., Eisenreich, S. A., Eds.; Advances in Chemistry 216; American Chemical Society: Washington, DC, 1987; pp 319–364.
- (73) Smith, J. N. *J. Environ. Radioact.* **2001**, *55*, 121–123.
- (74) Robbins, J. A. *Great Lakes regional fallout source functions*; Great Lakes Environmental Research Laboratory Technical Memo; ERL-GLERL-56; 1986; 21 pp.
- (75) Robbins, J. A.; Eadie, J. *Geophys. Res.* **1991**, *96*, 17081–17104.
- (76) Robbins, J. A.; Holmes, C.; Halley, R.; Bothner, M.; Shinn, E.; Graney, J.; Keeler, G.; tenBrink, M.; Orlandini, K. A.; Rudnick, D. *J. Geophys. Res.* **2000**, *105*, 28805–28821.
- (77) Van Hoof, P. L.; Andren, A. W. *J. Environ. Radioact.* **1989**, *55*, 121–123.
- (78) Carter, M. W.; Moghissi, A. A. *Health Phys.* **1977**, *33*, 55–71.
- (79) Schneider, A. R.; Stapelton, H. M.; Cornwell, J.; Baker, J. E. *Environ. Sci. Technol.* **2001**, *35*, 3809–3815.
- (80) Russell, R. W.; Gobas, F. A. P. C.; Haffner, G. D. *Environ. Sci. Technol.* **1999**, *33*, 416–420.
- (81) Durham, R. W.; Oliver, B. G. *J. Great Lakes Res.* **1983**, *9*, 160–168.
- (82) Wong, C. S.; Sanders, G.; Engstrom, D. R.; Long, D. T.; Swackhammer, D. L.; Eisenreich, S. J. *Environ. Sci. Technol.* **1995**, *29*, 2661–2672.
- (83) Howdshell, M. J.; Hites, R. A. *Environ. Sci. Technol.* **1996**, *30*, 969–974.
- (84) Huang, C. L.; Harrison, B. K.; Madura, J.; Dolfing, J. *Environ. Toxicol. Chem.* **1996**, *15*, 824–836.
- (85) Cook, P. M.; Zabel, E. W.; Peterson, R. E. In *Chemically-Induced Alterations in the Functional Development and Reproduction of Fishes*; Rolland, R., Gilbertson, M., Peterson, R., Eds.; SETAC Press: Pensacola, FL, 1997; Chapter 2, pp 9–27.
- (86) Environment Canada. *Toxic Chemicals in the Great Lakes and Associated Effects. Vol. 1. Contaminant Levels and Trends*; Ministry of Supplies and Services: Canada, 1991.
- (87) Simonen, H.; Skea, J.; Dean, H.; Symula, J. In *Proceedings of the Roundtable on Contaminant-Caused Reproductive Problems in Salmonids*; Driker, S., et al., Eds.; Special Publication of Great Lakes Fishery Commission; International Joint Commission: Windsor, ON, 1991.
- (88) Huestis, S. Y.; Servos, M. R.; Whittle, D. M.; Van den Heuvel, M.; Dixon, D. G. *Environ. Toxicol. Chem.* **1997**, *16*, 154–164.
- (89) Hornung, M. W.; Zabel, E. W.; Peterson, R. E. *Toxicol. Appl. Pharmacol.* **1996**, *140*, 227–234.
- (90) Tietge, J. E.; Johnson, R. D.; Jensen, K. M.; Cook, P. M.; Elonen, G. E.; Fernandez, J. D.; Holcombe, G. W.; Lothenbach, D. B.; Nichols, J. W. *Environ. Toxicol. Chem.* **1998**, *17*, 2395–2407.
- (91) O'Gorman, R.; Elrod, J. H.; Schneider, C. P. *J. Great Lakes Res.* **1998**, *24*, 131–144.
- (92) Baldwin, N. S.; Saalfeld, R. W.; Ross, M. A.; Buettner, H. J. *Commercial Fish Production in the Great Lakes 1867–1977*; Great Lakes Fishery Commission Technical Report 3; 1979.
- (93) Hornung, M. W.; Spitsbergen, J. M.; Peterson, R. E. *Toxicol. Sci.* **1999**, *47*, 40–51.
- (94) Cook, P. M.; Hornung, M. W.; Fredenburg, W.; Lawonn, M. J.; Loeffler, I. K.; Peterson, R. E. *Abstracts, 21st Annual Meeting of the Society of Environmental Toxicology and Chemistry*, Nashville, TN, November 12–16, 2000.
- (95) Carvalho, P. S.; Noltie, D.; Tillitt, D. E. *22nd Annual Meeting of the Society of Environmental Toxicology and Chemistry*, Baltimore MD, November 11–15, 2001.
- (96) Baird, O. E.; Kreuger, C. C. *J. Great Lakes Res.* **2000**, *26*, 141–151.
- (97) Hansen, M. J.; Peck, J. W.; Schorffhaar, R. G.; Selgeby, J. H.; Schreiner, D. R.; Schram, S. T.; Swanson, B. L.; MacCallum, W. R.; Burnham-Curtis, M. K.; Curtis, G.; Heinrich, J. W.; Young, R. J. *J. Great Lakes Res.* **1995**, *21* (Suppl. 1), 152–175.
- (98) Gilbertson, M. *Chemosphere* **1983**, *12*, 357–370.

Received for review January 15, 2003. Revised manuscript received April 21, 2003. Accepted June 4, 2003.

ES034045M